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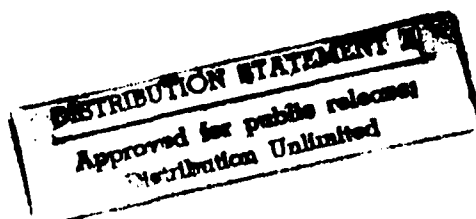


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**HEMATOLOGICAL EFFECTS OF 7.5% NaCl/6% DEXTRAN-70
(HSD) IN RABBITS AND PIGS**

Michael A. Dubick and James J. Summary

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The present study furthers our evaluation of the hematological effects of 7.5% NaCl/6% Dextran (HSD). Blood was obtained from both euvoletic and hemorrhaged rabbits and pigs at times up to 7 d after infusion of 4 ml/kg HSD. Complete blood counts and platelet concentrations were determined, and qualitative red blood cell (RBC) morphology was evaluated. In both species changes in hematocrit, hemoglobin, RBC, and platelet concentrations reflected the degree of hemorrhage and the subsequent plasma volume expansion induced by HSD. Infusion of HSD did not significantly affect mean corpuscular volume, mean corpuscular hemoglobin or mean corpuscular hemoglobin concentration and was consistent with the lack of significant morphological changes in RBC size, shape and staining intensity. Interestingly, a transient increase in white blood cell concentrations was observed, and at 2 to 4 hr after HSD infusion, a marked increase in segmented neutrophils was observed. In general, these data do not suggest any HSD-induced anemia, but they do support other observations that HSD infusion should have minimal effects on hemostasis.					
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ABSTRACT

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**Hematological Effects of 7.5% NaCl/6% Dextran-70
(HSD) in Rabbits and Pigs -- M. Dubick, J. Summary**

INTRODUCTION

The past decade has seen expanded research interest into the development of small-volume hypertonic/hyperoncotic solutions for the treatment of hemorrhagic hypotension. In particular, attention has been directed toward evaluating the safety and efficacy of 7.5% NaCl/6% Dextran-70 (HSD) in animal models of hemorrhage (1-4). HSD has been shown effective in restoring cardiovascular and renal function and tissue blood flow, thereby improving survival in potential lethal hemorrhage models in experimental animals (2,5,6). However, before HSD can be acceptable for human use, questions regarding its potentially adverse effects must be addressed. Of major concern are reports from experimental animals and humans that dextrans can interfere with blood clotting mechanisms (7-9). In addition, dextrans have been reported to interfere with the typing and cross-matching of red cells (10,11). In general, these effects are related to the molecular weight of the dextrans and the total dose infused (7,12,13). In our previous studies in hemorrhaged rabbits and pigs, HSD infused at the proposed therapeutic dose of 4 ml/kg did not significantly affect blood clotting or platelet aggregation (14,15). In addition, these same variables and red cell typing were not affected in human blood incubated with HSD (16,17). To more completely understand the blood picture following hemorrhage and HSD infusion, the present study reports on the complete blood cell analysis and red cell morphology assessed in hemorrhaged rabbits and pigs infused with HSD.

MATERIALS AND METHODS

Animals and Experimental Protocol

Adult, female New Zealand white rabbits (Elkhorn Rabbitry, Watsonville, CA) were randomly assigned to either the hemorrhage (n=5) or control (euolemic) (n=6) group. Conscious rabbits were hemorrhaged about 11% of blood volume as previously described (18). After a 30 min stabilization period, rabbits in both groups were infused i.v. with 4 ml/kg HSD. Blood samples were withdrawn prior to and 0.17, 0.5, 1, 2, 4, 24, 48, 72 and 96 h after infusion.

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Immature female Yorkshire pigs (n=20) weighing 25.2 ± 1.4 kg were randomly assigned to either the euvoletic control or hemorrhaged group. On the day of experiment, after a 1 h baseline period, pigs were bled 27 ml/kg body weight over a 60 min period. HSD was infused at 4 ml/kg. Blood samples were collected at the end of hemorrhage and at 0.5, 1, 2, 3, 4, 24, 48, 72, and 168 h after infusion. Other details of the experimental procedure and animal husbandry and surgery have been described (2,15).

Hematology Evaluation

Hematology values were determined by a standard complete blood count using a Baker 9000 Blood Cell Analyzer. These variables included the red blood cell count (RBC), red blood cell indices [mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH) and mean corpuscular hemoglobin concentration (MCHC)], hemoglobin, hematocrit, white blood cell count (WBC) and platelet count. In addition, a blood smear was stained with Wright's Stain and a microscopic examination for red cell morphology and white cell differential count was performed.

Statistical Analysis

Data were analyzed by 1-way ANOVA with time as the variable or by 2-way ANOVA with time and treatment (hemorrhage) as variables. Differences between the means were further evaluated by Dunnett's test. A $p < 0.05$ was considered statistically significant.

RESULTS

In rabbits, HSD infusion resulted in a 15 to 17% reduction in hematocrit and hemoglobin concentrations in both the hemorrhaged and non-hemorrhaged groups (Table 1). These groups also showed a significant decrease in RBC concentrations compared with baseline, at all times following HSD infusion (Table 1). At all times after HSD infusion, RBC concentrations were significantly lower in the hemorrhaged than euvoletic rabbits (Table 1). In general this decrease was proportional to the change in hematocrit or

hemoglobin concentrations observed after HSD infusion. At no time, however, was MCV, MCH, or MCHC significantly affected by HSD infusion in either group (Table 1).

WBC concentrations in rabbits were significantly higher than baseline at 24, 48 and 72 hr after HSD infusion in the hem+HSD group, but returned to baseline values by 7 d (Table 2). In both groups the percentage of segmented neutrophils and lymphocytes was significantly higher than baseline at 2 hr and 4 hr after infusion (Table 2). This translated into a 2-3 fold increase in absolute number of segmented neutrophils from 1 to 72 hr in the hem+HSD group, whereas the increase in these cells was less in the euvoletic group during this same time period. No significant change in the number of lymphocytes were observed, except at 48 and 72 hr in the hem+HSD group. It should be noted that monocytes were 2% or less at baseline and throughout the experimental period. Platelet concentrations decreased in both groups after HSD infusion, similar to the decrease in hematocrit (Table 2). However, statistically lower concentrations were only observed in the hem+HSD group at 4 and 24 hr after HSD infusion. Platelet concentrations were similar to pre-infusion values by 48 hr after HSD administration.

HSD infusion also induced minimal change in RBC morphology in each group (data not shown). Slight Rouleaux formation was observed in one rabbit from each group.

Following HSD infusion, hemoglobin concentrations and hematocrit observed were more greatly decreased in hemorrhaged pigs compared with rabbits, reflecting the greater degree of hemorrhage and larger plasma volume expansion in the pigs (Table 3). HSD infusion also resulted in a significant decrease in RBC concentrations in hemorrhaged pigs, whereas no significant decrease was observed in euvoletic swine (Table 3). Within the hemorrhaged or euvoletic groups, no significant changes were observed in MCV, MCH, nor MCHC following HSD infusion, but MCV and MCH were significantly different between both groups at all times following HSD infusion (Table 3).

Total WBC concentrations in pigs were not significantly affected by hemorrhage or HSD infusion (Table 4). The percentage of segmented

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neutrophils was significantly higher than baseline in the hemorrhaged pigs at 2, 3, and 4 hr after HSD infusion, similar to the effect seen in rabbits. Consequently, the percentage of lymphocytes was significantly lower in the hemorrhaged group for the first 4 hr following HSD infusion (Table 4). These changes in the percentage of segmented neutrophils and lymphocytes translated into a 2-fold increase in segmented neutrophils during this time period in both groups. This change in the number of neutrophils was accompanied by a 25%-50% decrease in lymphocytes in both groups, 2-4 hr after HSD infusion. As in the rabbits, no monocytes were observed in the pig white cell differential count. HSD infusion did not significantly affect platelet concentrations in either hemorrhaged or euvoletic pigs (Table 4). The decreased concentrations reflected the change in hematocrit due to the volume expansion following HSD infusion.

Given the natural tendency for swine RBC's to crenate, morphological changes following HSD infusion were only qualitatively evaluated. No consistent alterations in cell size, shape, or staining intensity were noted in either group after HSD infusion.

DISCUSSION

Previous reports that early clinical dextran solutions could interfere with platelet aggregation and thereby affect blood coagulation (7-9), raised much concern about the potentially adverse hematological effects of HSD. It was also suggested that plasma clotting factors, already reduced as a result of hemorrhage, could be further diluted by the volume expansion induced by HSD. In addition, an individual who received HSD for severe blood loss and survived to an emergency room would be a candidate for blood transfusions. The potential for dextrans to induce RBC aggregation (10) could potentially interfere with typing and cross-matching.

In the present studies with rabbits and swine, RBC parameters measured were consistent with previous data published for rabbits and swine (19). It was observed that, consistent with the decrease in hematocrit and hemoglobin concentrations, changes in RBC concentrations reflected the loss

of red cells with hemorrhage and the plasma volume expansion following HSD infusion. In swine, after HSD infusion, the greater decrease in RBC concentrations in the hemorrhaged than euvoletic group reflects the larger blood loss and greater plasma volume expansion than that which occurred in rabbits. The further reduction in hematocrit and hemoglobin concentrations 24 hr after HSD infusion in both species, reflects the fact that after the initial 4 hr experimental period, the animals were returned to their cages and allowed free access to food and water. This effect of eating and drinking on hematocrit and hemoglobin concentration has been a consistent observation 24 hr after HSD administration (3,15).

The current studies also did not detect any significant changes in MCV, MCH, and MCHC after HSD infusion. These observations agree with the lack of consistent HSD-induced morphological changes in RBC size, shape, or staining intensity.

In the present study, WBC concentrations of both species of animals slightly increased over the 7 d experimental period although statistical significance was achieved at only a few of the later time points. In the swine, baseline WBC concentrations were higher than previously published data for normal minipigs (19). Although all surgeries in swine were performed under aseptic conditions and animals were treated with antibiotics post-operatively, a low-grade infection could have developed during the 2 wk following the surgery, and the subsequent repeated opening of catheters for fluid infusion and blood withdrawal. However, it should be noted that less surgical procedures and catheterizations were performed in rabbits than pigs, yet rabbits had a greater increase in WBC concentrations than pigs. Therefore, it does not appear that change in WBC concentrations can be solely accounted for by a possible presence of infection. In rabbits, an increase in WBC concentrations over baseline was only observed at 24, 48, and 72 hr in the hem+HSD group. By 7 d, WBC concentrations had returned to baseline levels. It should be noted, however, that in acute and subacute toxicity studies in which HSD was administered to rabbits daily for up to 14 d at the maximum tolerated dose (16 ml/kg), no increase in WBC's was observed (20,21). Consistent with the present data, it has been observed in humans that acute blood loss causes a rise in the WBC count (22). However, in the few studies reported in the literature dextran infusion had no consistent effect on WBC concentrations (8).

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Interestingly, from 2 hr to 4 hr after HSD infusion, a marked increase in the percentage of segmented neutrophils and a subsequent decrease in the percentage of lymphocytes was observed in both rabbits and pigs and this effect was independent of hemorrhage. No consistent changes in these WBC's were observed in acute or subacute toxicity studies of HSD in rabbits (20, 21), but the 2-4 hr time period was not assayed in these studies. In the present studies, the higher percentage of segmented neutrophils translated into higher absolute numbers of these WBC's. It is possible that the increased WBC concentrations seen result from demargination of granulocytes in both rabbits and pigs. This is a common observation following hormonal stimulation or general trauma or stress as might be associated with animal handling and hemorrhage. Confirmation that the increased WBC concentrations relate more to the experimental procedure than HSD infusion could be confirmed in hemorrhaged animals not infused with HSD or in euvoletic animals infused with normal saline.

Platelet concentrations in the current rabbit study are consistent with previously published data, whereas in the current pig study, baseline platelet concentrations were about 2-fold higher than previously published normal hematological values for minipigs (19). Nevertheless, in both experimental groups and in both species, decreases in platelet concentrations reflected the volume expansion induced by HSD. Although high concentrations of dextran are known to decrease platelet aggregation and increase bleeding times (8,9,16,23), the present data suggest that platelet concentrations are not markedly reduced enough to contribute to adverse effects of high dextran or salt concentrations on coagulation (8,9,24).

The lack of significant Rouleaux formation or platelet or WBC clumping in the present study is an important finding. Previous studies have suggested that as a rule, Dextran-70 aggregates RBC's and platelets (8). It has been suggested that these aggregated cells, if sequestered in the lung, could lead to events responsible for dextran induced anaphylactoid reactions (25). The lack of HSD-induced RBC, platelet or WBC clumping in the present and our previous studies with human blood (16,17), further support our observations that no immunological abnormalities were observed in acute and subacute toxicity studies with HSD (26).

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In conclusion, the present data do not support any concerns that HSD induces anemia or significantly alters RBC morphology that could interfere with typing and crossmatching. Taken together with recent observations that HSD, at the proposed therapeutic dose of 4 ml/kg does not interfere with blood clotting, bleeding times or platelet aggregation (15), and the paucity of hematological effects in acute and subacute toxicity studies with HSD (20,21), these data imply that the efficacy of HSD for the prehospital treatment of hemorrhagic hypotension will not be compromised by problems of impaired hemostasis.

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TABLE 1

Effect of HSD Infusion on Red Blood Cell Parameters in Rabbits

Time		RBC ($\times 10^6$)	HGB (g/dl)	Hct (%)	MCV (μm^3)	MCH (pg)	MCHC (g/dl)
Baseline	Hem+HSD	5.9 $\pm$ 0.2	11.4 $\pm$ 1.1	37.4 $\pm$ 0.6	64.1 $\pm$ 0.9	21.2 $\pm$ 0.3	33.1 $\pm$ 0.6
	HSD	6.2 $\pm$ 0.3	13.1 $\pm$ 0.6	38.6 $\pm$ 1.4	63.4 $\pm$ 1.2	21.0 $\pm$ 0.5	33.1 $\pm$ 0.3
Post-hemorrhage	Hem+HSD	5.1 $\pm$ 0.1	11.1 $\pm$ 0.2	33.5 $\pm$ 0.7	65.7 $\pm$ 0.7	21.8 $\pm$ 0.3	33.2 $\pm$ 0.7
	HSD						
0.17 hr	Hem+HSD	4.4 $\pm$ 0.2*	9.4 $\pm$ 0.3	27.9 $\pm$ 0.7*	64.4 $\pm$ 1.0	21.6 $\pm$ 0.4	33.5 $\pm$ 0.3
	HSD	5.1 $\pm$ 0.2*	10.7 $\pm$ 0.4*	32.4 $\pm$ 1.4	63.6 $\pm$ 1.2	21.0 $\pm$ 0.5	33.1 $\pm$ 0.3
0.5 hr	Hem+HSD	4.4 $\pm$ 0.2*	9.6 $\pm$ 0.3*	28.6 $\pm$ 1.1*	64.7 $\pm$ 1.0	21.8 $\pm$ 0.5	33.6 $\pm$ 0.3
	HSD	5.3 $\pm$ 0.2	11.1 $\pm$ 0.4	33.6 $\pm$ 1.4	53.6 $\pm$ 9.3	21.0 $\pm$ 0.5	33.0 $\pm$ 0.3
1.0 hr	Hem+HSD	4.3 $\pm$ 0.2*	9.3 $\pm$ 0.3*	28.0 $\pm$ 1.0*	64.7 $\pm$ 1.0	21.6 $\pm$ 0.4	33.3 $\pm$ 0.4
	HSD	5.2 $\pm$ 0.2	10.8 $\pm$ 0.5	33.2 $\pm$ 1.4	64.4 $\pm$ 1.3	21.0 $\pm$ 0.5	32.7 $\pm$ 0.1
2.0 hr	Hem+HSD	4.4 $\pm$ 0.2*	9.5 $\pm$ 0.3*	28.0 $\pm$ 1.0*	64.6 $\pm$ 1.1	20.2 $\pm$ 1.3	31.2 $\pm$ 1.8
	HSD	4.9 $\pm$ 0.3*	10.2 $\pm$ 0.5*	30.9 $\pm$ 1.5*	63.7 $\pm$ 1.2	21.1 $\pm$ 0.5	33.1 $\pm$ 0.2
4.0 hr	Hem+HSD	3.9 $\pm$ 0.2*	8.6 $\pm$ 0.4*	25.4 $\pm$ 1.0*	64.7 $\pm$ 1.0	21.9 $\pm$ 0.3	33.8 $\pm$ 0.4
	HSD	4.9 $\pm$ 0.3*	10.3 $\pm$ 0.8	30.8 $\pm$ 2.4*	63.3 $\pm$ 1.5	21.2 $\pm$ 0.5	33.4 $\pm$ 0.2
24 hr	Hem+HSD	3.5 $\pm$ 0.2*	7.5 $\pm$ 0.4*	22.9 $\pm$ 1.0*	65.3 $\pm$ 0.9	21.4 $\pm$ 0.5	32.8 $\pm$ 0.7
	HSD	4.1 $\pm$ 0.3*	8.8 $\pm$ 0.7*	26.4 $\pm$ 2.1	63.9 $\pm$ 1.2	21.3 $\pm$ 0.3	33.4 $\pm$ 0.6
48 hr	Hem+HSD	3.3 $\pm$ 0.2*	7.3 $\pm$ 0.4	21.4 $\pm$ 0.9*	67.2 $\pm$ 1.2	22.8 $\pm$ 0.3	34.0 $\pm$ 0.6
	HSD	3.9 $\pm$ 0.3*	8.7 $\pm$ 0.8*	25.6 $\pm$ 2.5*	65.0 $\pm$ 1.4	22.1 $\pm$ 0.2	34.1 $\pm$ 0.8
72 hr	Hem+HSD	3.1 $\pm$ 0.2*	7.4 $\pm$ 0.4*	22.0 $\pm$ 1.0*	71.5 $\pm$ 2.0	23.8 $\pm$ 0.7	33.4 $\pm$ 0.2
	HSD	4.2 $\pm$ 0.4*	9.2 $\pm$ 1.2	27.4 $\pm$ 3.3	65.6 $\pm$ 1.6	22.0 $\pm$ 0.6	33.5 $\pm$ 0.3
168 hr	Hem+HSD	4.5 $\pm$ 0.2*	9.2 $\pm$ 1.2	31.6 $\pm$ 1.6	70.4 $\pm$ 1.5	20.5 $\pm$ 2.3	29.0 $\pm$ 2.7
	HSD	4.5 $\pm$ 0.2*	10.2 $\pm$ 0.7	30.8 $\pm$ 2.0	68.2 $\pm$ 2.4	22.4 $\pm$ 0.7	32.9 $\pm$ 0.3

Data expressed as mean $\pm$ S.E. for 5-6 animals per group

*p<0.05 from corresponding baseline value

TABLE 2

Effect of HSD Infusion on White Blood Cells and Platelets in Rabbits

Time		WBC ($\times 10^3$)	SEG (%)	LYMPH (%)	PLT ($\times 10^3$)
Baseline	Hem+HSD HSD	6.1 $\pm$ 0.4 7.2 $\pm$ 1.6	34 $\pm$ 6 36 $\pm$ 6	64 $\pm$ 6 62 $\pm$ 7	406 $\pm$ 24 437 $\pm$ 28
Post-hemorrhage	Hem+HSD HSD	6.1 $\pm$ 0.4	45 $\pm$ 4	53 $\pm$ 4	410 $\pm$ 36
0.17 hr	Hem+HSD HSD	6.5 $\pm$ 0.8 5.9 $\pm$ 1.0	49 $\pm$ 6 45 $\pm$ 7	48 $\pm$ 7 55 $\pm$ 7	316 $\pm$ 22 340 $\pm$ 40
0.5 hr	Hem+HSD HSD	6.6 $\pm$ 1.3 6.1 $\pm$ 1.1	51 $\pm$ 8 56 $\pm$ 5	47 $\pm$ 8 43 $\pm$ 5	328 $\pm$ 24 366 $\pm$ 27
1.0 hr	Hem+HSD HSD	8.6 $\pm$ 1.3 7.0 $\pm$ 1.1	58 $\pm$ 7 56 $\pm$ 5	42 $\pm$ 7 43 $\pm$ 5	331 $\pm$ 22 317 $\pm$ 63
2.0 hr	Hem+HSD HSD	8.1 $\pm$ 0.8 7.8 $\pm$ 0.9	64 $\pm$ 7* 63 $\pm$ 5*	36 $\pm$ 6* 36 $\pm$ 5*	342 $\pm$ 16 336 $\pm$ 20
4.0 hr	Hem+HSD HSD	7.7 $\pm$ 0.3 9.2 $\pm$ 1.6	66 $\pm$ 5* 64 $\pm$ 5*	34 $\pm$ 5* 35 $\pm$ 5*	289 $\pm$ 32 326 $\pm$ 29
24 hr	Hem+HSD HSD	10.1 $\pm$ 1.2 10.4 $\pm$ 1.1	47 $\pm$ 7 58 $\pm$ 5	52 $\pm$ 7 40 $\pm$ 5	253 $\pm$ 43 317 $\pm$ 41
48 hr	Hem+HSD HSD	14.5 $\pm$ 1.3 11.0 $\pm$ 1.5	39 $\pm$ 5 46 $\pm$ 9	60 $\pm$ 5 53 $\pm$ 8	332 $\pm$ 54 393 $\pm$ 54
72 hr	Hem+HSD HSD	17.4 $\pm$ 2.9 8.5 $\pm$ 1.6	39 $\pm$ 6 42 $\pm$ 1	60 $\pm$ 6 57 $\pm$ 1	378 $\pm$ 67 449 $\pm$ 40
168 hr	Hem+HSD HSD	5.9 $\pm$ 0.3 5.9 $\pm$ 0.9	38 $\pm$ 12 45 $\pm$ 4	61 $\pm$ 11 51 $\pm$ 4	563 $\pm$ 30 594 $\pm$ 76

*Data expressed as mean $\pm$ S.E. for 5-6 animals/group
*p<0.05 from corresponding baseline value

TABLE 3

Effect of HSD Infusion on Red Blood Cell Parameters in Swine¹

Time		RBC (x10 ⁶)	HGB (g/dl)	Hct (%)	MCV (μ m ³)	MCH (pg)	MCHC (g/dl)
Baseline	Hem+HSD HSD	6.1 $\pm$ 0.1 6.3 $\pm$ 0.2	9.7 $\pm$ 0.2 9.1 $\pm$ 0.3	30.8 $\pm$ 0.5 29.3 $\pm$ 0.9	50.5 $\pm$ 0.5 46.8 $\pm$ 1.2†	15.9 $\pm$ 0.2 14.6 $\pm$ 0.5	31.5 $\pm$ 0.2 31.1 $\pm$ 0.4
Post-hemorrhage	Hem+HSD HSD	5.6 $\pm$ 0.4	8.8 $\pm$ 0.7	28.4 $\pm$ 2.3	50.6 $\pm$ 0.5	15.7 $\pm$ 0.2	31.0 $\pm$ 0.2
0.5 hr	Hem+HSD HSD	4.2 $\pm$ 0.1* 5.8 $\pm$ 0.2†	6.7 $\pm$ 0.2* 8.3 $\pm$ 0.3*	21.4 $\pm$ 0.7* 27.0 $\pm$ 0.8†	50.9 $\pm$ 0.5 46.8 $\pm$ 1.3†	16.0 $\pm$ 0.3 14.4 $\pm$ 0.5†	31.5 $\pm$ 0.4 30.7 $\pm$ 0.4
1.0 hr	Hem+HSD HSD	4.3 $\pm$ 0.1* 5.8 $\pm$ 0.2	6.9 $\pm$ 0.2* 8.2 $\pm$ 0.3	22.0 $\pm$ 0.7† 26.6 $\pm$ 0.8	50.9 $\pm$ 0.5 46.2 $\pm$ 1.3*	16.1 $\pm$ 0.3 14.3 $\pm$ 0.4	31.6 $\pm$ 0.4 31.0 $\pm$ 0.4
2.0 hr	Hem+HSD HSD	4.4 $\pm$ 0.2* 6.0 $\pm$ 0.2	7.1 $\pm$ 0.3* 8.8 $\pm$ 0.3	22.5 $\pm$ 1.8* 27.9 $\pm$ 0.8	50.8 $\pm$ 0.5 46.6 $\pm$ 1.3	16.0 $\pm$ 0.3 14.7 $\pm$ 0.5	31.5 $\pm$ 0.4 31.6 $\pm$ 0.4
3.0 hr	Hem+HSD HSD	4.4 $\pm$ 0.2* 6.0 $\pm$ 0.2	7.0 $\pm$ 0.3* 8.8 $\pm$ 0.3	22.0 $\pm$ 0.8* 28.1 $\pm$ 0.8	50.5 $\pm$ 0.5 46.8 $\pm$ 1.4	16.0 $\pm$ 0.3 14.7 $\pm$ 0.5	31.6 $\pm$ 0.3 31.3 $\pm$ 0.4
4.0 hr	Hem+HSD HSD	4.2 $\pm$ 0.2* 6.0 $\pm$ 0.2	6.7 $\pm$ 0.3* 8.7 $\pm$ 0.2	21.2 $\pm$ 1.1* 27.7 $\pm$ 0.8	50.4 $\pm$ 0.5 46.6 $\pm$ 1.2	19.7 $\pm$ 3.8 14.7 $\pm$ 0.5	31.6 $\pm$ 0.4 31.4 $\pm$ 0.5
24 hr	Hem+HSD HSD	3.5 $\pm$ 0.1* 5.9 $\pm$ 0.2	5.5 $\pm$ 0.2* 8.6 $\pm$ 0.3	17.7 $\pm$ 0.8* 27.6 $\pm$ 1.0	50.9 $\pm$ 0.7 47.1 $\pm$ 1.2	15.9 $\pm$ 0.7 14.6 $\pm$ 0.4	31.3 $\pm$ 0.4 31.0 $\pm$ 0.6
48 hr	Hem+HSD HSD	3.5 $\pm$ 0.1* 5.7 $\pm$ 0.1	5.7 $\pm$ 0.2* 8.2 $\pm$ 0.3	18.4 $\pm$ 0.5* 26.5 $\pm$ 0.7	51.8 $\pm$ 0.3 46.9 $\pm$ 1.1	16.1 $\pm$ 0.4 14.6 $\pm$ 0.5	31.2 $\pm$ 0.7 31.0 $\pm$ 0.4
72 hr	Hem+HSD HSD	3.6 $\pm$ 0.1* 5.6 $\pm$ 0.2	6.0 $\pm$ 0.1* 8.2 $\pm$ 0.3	18.9 $\pm$ 0.5* 26.6 $\pm$ 0.9	52.9 $\pm$ 0.7 47.3 $\pm$ 1.1	16.7 $\pm$ 0.2 14.6 $\pm$ 0.5	31.7 $\pm$ 0.2 30.9 $\pm$ 0.5
168 hr	Hem+HSD HSD	4.2 $\pm$ 0.2* 5.5 $\pm$ 0.2	6.7 $\pm$ 0.4* 8.1 $\pm$ 0.4	22.1 $\pm$ 1.5* 26.2 $\pm$ 1.3	52.3 $\pm$ 1.1 47.2 $\pm$ 1.1	15.9 $\pm$ 0.4 14.7 $\pm$ 0.5	30.3 $\pm$ 0.3 31.2 $\pm$ 0.6

¹Data expressed as mean $\pm$ S.E. Hem + HSD group, n=9; HSD group n=11

*p<0.05 from baseline and post-hemorrhage value

† p<0.05 from Hem + HSD group at all times after HSD infusion

TABLE 4

Effect of HSD Infusion on White Blood Cells and Platelets in Swine¹

Time		WBC (x10 ³)	SEGS (%)	LYMPH (%)	PLT (x10 ³)
Baseline	Hem+HSD HSD	27.2±2.6 32.7±2.6	57±6 72±4	34±4 23±4	638±63 575±48
Post-hemorrhage	Hem+HSD HSD	24.5±3.3	54±8	35±6	450±62
0.5 hr	Hem+HSD HSD	29.3±6.7 27.7±3.2	70±6 72±4	24±5* 24±4	467±42 510±42
1.0 hr	Hem+HSD HSD	33.5±6.1 31.6±3.1	78±4 79±3	13±3* 17±2	453±42 523±42
2.0 hr	Hem+HSD HSD	36.5±6.1 36.7±2.6	82±3* 79±4	13±3* 16±3	477±41 547±40
3.0 hr	Hem+HSD HSD	35.2±5.6 38.2±2.3	84±3* 84±2*	12±3* 13±2	484±48 581±46
4.0 hr	Hem+HSD HSD	36.4±4.9 39.7±3.9	84±2* 81±2*	12±2* 13±2	489±51 555±39
24 hr	Hem+HSD HSD	28.9±2.5 36.3±2.2	54±4 65±4	35±3 31±4	432±33 514±70
48 hr	Hem+HSD HSD	33.3±3.8 43.7±2.9	53±6 67±4	40±5 27±3	453±52 566±39
72 hr	Hem+HSD HSD	31.8±4.2 42.8±2.8	55±8 69±5	35±6 26±5	630±51 519±51
168 hr	Hem+HSD HSD	30.0±2.4 44.7±2.8	64±6 71±3	31±6 26±3	624±55 575±48

¹Data expressed as mean ± S.E. Hem + HSD group n=9, HSD group n=11.

*p<0.05 from baseline and post-hemorrhage values.